

N-TERMINAL

| | | | | | | | | | | | | | | | |
|---------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|---|
| P26h | MK | LN | FS | XL | RA | LV | TG | AG | KG | IG | IG | XD | TA | KA | L |
| Adipsin | -- | -- | -- | G- | -- | -- | -- | -- | -- | -- | -- | R- | -V | -- | - |

NCS FRAGMENT

| | | | | | | | | | | | | | |
|---------|----|----|----|----|----|----|----|----|----|----|----|----|----|
| P26h | XA | TE | KA | LG | XI | GP | VX | XL | VN | NA | AL | XX | XQ |
| Adipsin | D- | -- | -- | -- | G- | -- | -D | L- | -- | -- | -- | VM | I- |

CNBr fragment

| | | | | | |
|---------|----|----|----|----|---|
| P26h | LY | PY | KX | RV | N |
| Adipsin | -G | -H | -I | -- | - |

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PCT/CA99/00437

WO 99/64064

1 2 3 4 5 6 7 8 9 10 11 12

1081 -

Cyclophilin

2/12

FIGURE - 2

| | |
|---|-----|
| GTCCCTGGAGGGTTGGCTGTAGGATTCAAGGTGGCTTCAAGGCTCAGGCTGGG | 47 |
| ATCAAGGACACAGTGAGGCAGATAACCTTAACCTCAGCCCTCCC | 92 |
| CTCGCCACAGGAGGACACTGGTGTCAAGCAGCATG AAG CTG AAT | 135 |
| M K L N | 4 |

TTC ACT GGT CTC AGG GCT CTG GTG ACC GGG GCA GGG AGA GGG
 F T G L R A L V T G A G R G

ATT GGG CGA GGC ACT GCG AAA GCC CTG CAT GCC TCA GGA GCC
 I G R G T A K A L H A S G A 219
 1 32

AAA GTG GTG GCC GTG TCA CTC ATC AAC GAA GAC CTC GTC AGC
 K V V A V S L I N E D L V S

CTTG GCC AAA GAG TGT CCG GGC ATA GAG CCT GTG TGT GTG GAC
L A K E C P G I E P V C V D

CTG GGT GAC TGG GAG GCC ACA GAG AAG GCA CTC GGG CGT ATT
L G D W E A T E K A L G R I 345 74

GGC CCC GTG GAC CTG CTG GTG AAC AAT GCG GCG GTG GCG CTA 387
G P V D L L V N N A A V A L 88

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| | | |
|--|-----|---------------|
| GTG CAG CCT TTCA TAC CAG TCT ACC AAG GAG GTC TTT GAC AGG | 429 | $\frac{4}{2}$ |
| V Q P F I Q S T K E V F D R | 102 | |
| TCCTTC AAT GTG AAT GTG CGCT TCT GTG CTG CAA GTG TCCC CAG | 471 | $\frac{4}{2}$ |
| S F N V N R S V L Q V S Q | 116 | |
| ATG GTA GCC AAG GGC ATG ATT AAC CGT GGA GTG GCA GGA TCC | 513 | $\frac{4}{2}$ |
| M V A K G M I N R G V A G S | 130 | |
| ATT GTC AAC ATCTCC AGC ATG GTG GCCTAT GTC ACC TTCC CCT | 555 | $\frac{4}{2}$ |
| I V N I S S M V A Y V T F P | 144 | |
| GGT CTG GCC ACG TAC AGC TCC ACC AAG GGT GCT ATA ACC ATG | 597 | $\frac{4}{2}$ |
| G L A T Y S S T K G A I T M | 158 | |
| CTG ACC AAA GCC ATG GAG ATG GTC GGA CCA TAC AAG ATC | 639 | $\frac{4}{2}$ |
| L T K A M A M E L G P Y K I | 172 | |
| CGG GTG AAC TCT GTA AAC CCT ACC GTC GCT ACT GAC ATG | 681 | $\frac{4}{2}$ |
| R V N S V N P T V L T D M | 186 | |
| GGC AAG AAA GTC TCT GCA GAC CCG GAA TTT GCC AAG AAG CTC | 723 | $\frac{4}{2}$ |
| G K K V S A D P E F A K K L | 200 | |

75 - 3B

AAG GAG CGC CAC CCA CTG AGG AAG TTC GCA GAG GTG GAG GAC 765
K E R H P L R K F A E V E D 214

GTG GTC AAC AGC ATC CTC TTC CTG CTC AGC GAC AGC AGC GCC 807
V V N S I L F L L S D S S A 228

TCT ACC AGC GGCTCTGGCATCCTGCTGAGCTGGCTGGAGACTTCC 849
S T S G S G I L V D A G Y L 242

GCC TCC TAG ACGGCCAGGGACTCCTGGAGACTTCC 892
A S Amber 244

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12

CTGGCCTCACCTTACATCAAGACCCCCCTCAACCCAAATAAT 941
TTTGTTCGAATCCTGTAGAGCCCCACACATCCATCCCCAACT 990
TTAGACTCCGGATCCGATTCCATACCAGCTATGCTGAGATAATT 1038
TGATTAATAAGTATCCAAACCAACAAAAAA 1081

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| | |
|-------------|--|
| P26h | MK LN FT GL RA LV TG AG RG IG RG TA KA LH AS GA KV VA VS LI NE DL VS LA KE 50 |
| Adipsin | -- -- - S - - - - - - - - D - V - - - - - - T RT - S - - - - - - 50 |
| C.Reductase | - Q M- - S - - - - - - K- - - D - V - - - V- - - R- - - T RT - G - - - S Q- 50 |

| | |
|-------------|--|
| P26h | CP GI EP VC VD LG DWEA TE KA LG RI GP VD LL VN NA AV AL VQ PF IQ ST KE VF 100 |
| Adipsin | -- -- - - - - D - - - - G- - - - - - - L VI M- - - LE V- - - A- 100 |
| C.Reductase | -- -- - - - - - - R- - - GV - - - - - - - M- - - LD T- - - - 100 $\frac{6}{N}$ |

| | |
|-------------|---|
| P26h | DR SF NV NV RS VL QV SQ MV AK GMN RG VA GS IV NI SS MVAY VT FP GL AT YS 150 |
| Adipsin | -- -- S- - L - - F - - - - R D- - - - P - - - - V - - - - H - - - N- I- - - 150 |
| C.Reductase | -- -- - - L - - F - - - I- - R S- - E - - P - - - V - - - SH - - Y- - - A - - 150 |

| P26h | ST | KG | AI | TMLT | KA | MAME | LG | PY | KI | RV | NS | VN | PT | VV | LT | DMGK | KV | SA | DP | EF | AK | KL | 200 | |
|---------------------------|----|----|----|------|----|------|----|----|----|----|----|----|----|----|----|------|-----|----|----|----|----|----|-----|-----|
| Adipsin | -- | -- | -M | -- | - | - | - | - | - | -H | -- | - | - | - | - | - | - | - | - | - | - | - | 200 | |
| C ₁ -Reductase | -- | -- | -M | -- | - | -S | -- | -- | -H | -- | -- | -- | -- | -- | -- | -- | -A- | -R | S- | TS | -- | -L | -R | 200 |

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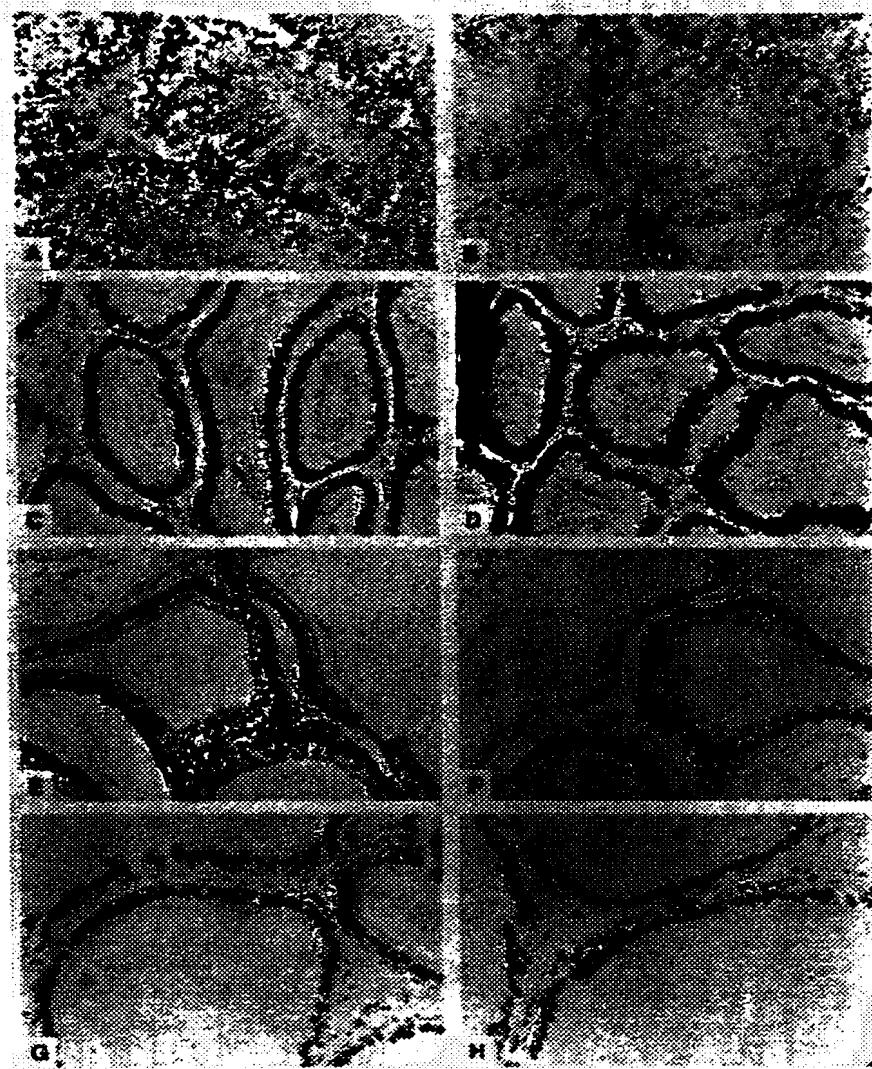
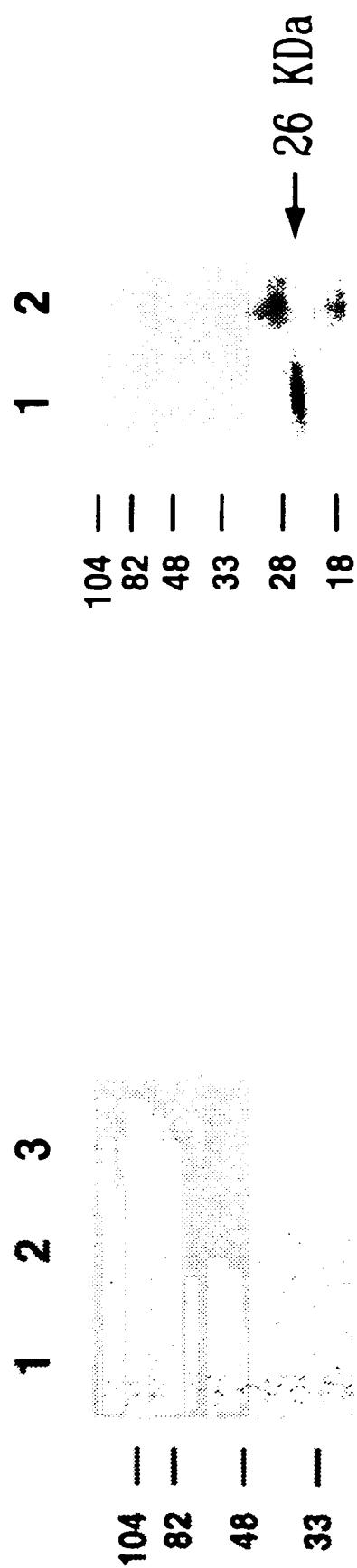
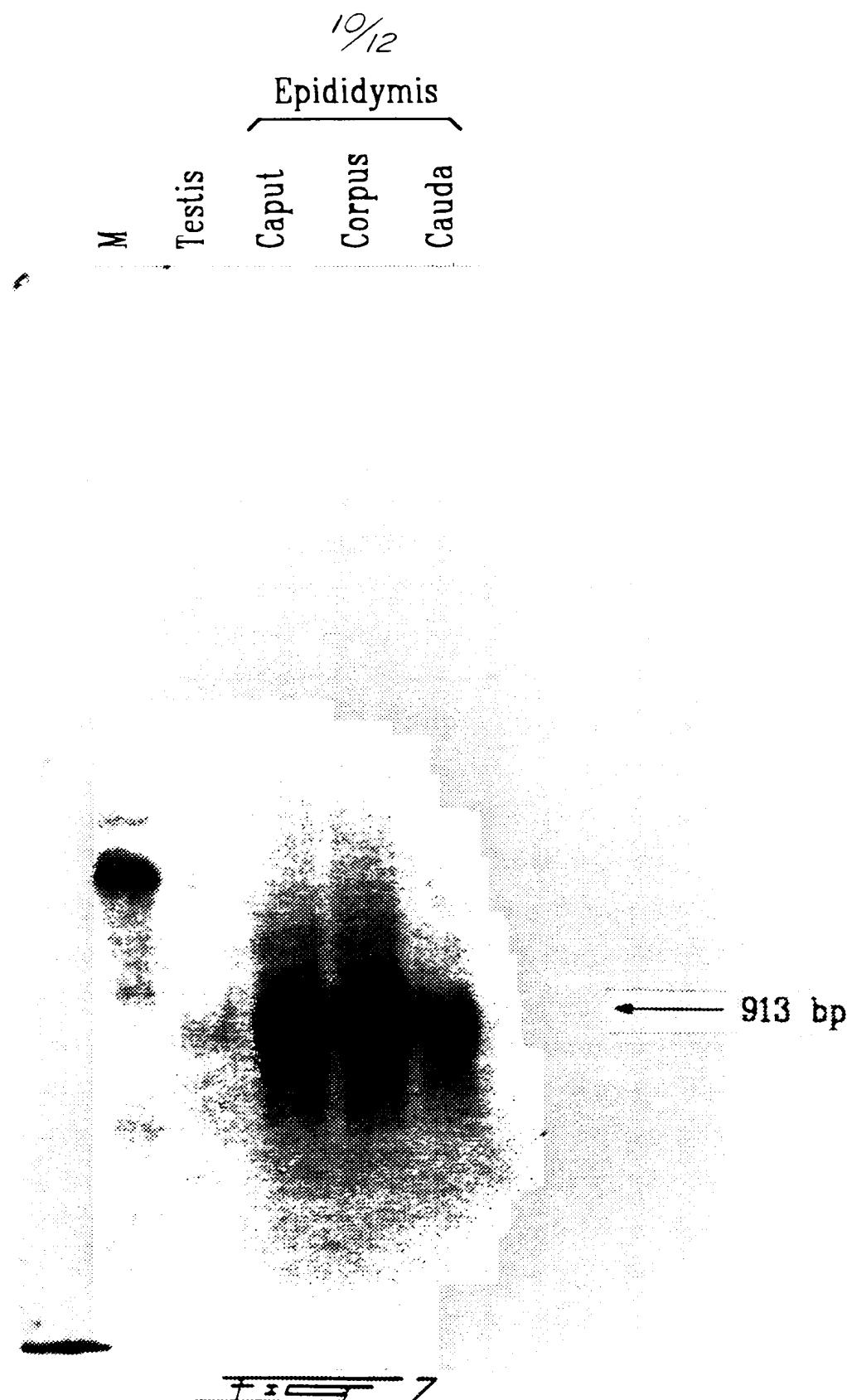


FIG-5

SUBSTITUTE SHEET (RULE 26)

9/12

757 - 6B757 - 6A



| | | | | | | | |
|----|-----|-----|-----|-----|-----|-----|-----|
| 90 | 100 | 110 | 120 | 130 | 140 | 150 | 160 |
| | | | | | | | |

— 8A —

170 180 190 200 210 220 230 240
 | | | | | | | |
 KAMAMELGPYKIRVNISVNPTVVLTDMGKRVSAADPEFAFLKIFERHPLRFKFAEVEDVVSILFLLSDSSAATSGSGILVDA
 •
 KVMALELGPHKIRVNNAVNPVVMTSMGQATWSDPHKAKTMLNRIPLGKFAEVETHVVNIAILFLLSDRSGMTIGSTLIPVERG
 | | | | | | | |
 170 180 190 200 210 220 230 240
 | | | | | | | |
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YLAS
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FWAC